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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/560,761	04/28/2000	Dean Della Penna	1095R	5179

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EXAMINER
SWITZER, JULIET CAROLINE

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/560,761	PENNA ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-26 and 31-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-26 and 31-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6/9/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is written in response to applicant's correspondence submitted 6/9/2003. Claims 22, 23, 25, 26 and 31-33 have been amended and claims 27, 28, 34, 35, and 36 have been cancelled. Claims 22-26 and 31-33 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not fully persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is final.**

Priority

2. For clarification, the first line of the specification recites that "This application is a CIP of U.S. Patent Application Serial No. 09/307460, filed May 7, 1999, now abandoned." The examiner's citation of 09/607460 in the previous office action was a typographical error.

Information Disclosure Statement

3. The newly filed IDS has been considered. A signed copy of the 1449 is enclosed herewith.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 22, 24, 25, 26, 31, and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 22, 24, 25, and 26, recite a method for modulating the level of tocopherol in a plant which comprise stably transforming a plant cell with a polynucleotide selected from (iii) a polynucleotide having 70% sequence identity to SEQ ID NO: 3 or (iv) a polynucleotide which selectively hybridizes to SEQ ID NO: 3 under "stringent conditions" and a given wash condition, or the complement of either of these polynucleotides. Claims 31 and 33 specify that the polynucleotide is that of option (iii) or (iv) respectively.

However, within the broad genus of nucleic acids encompassed for use in the claimed methods, the instant specification only describes a single polynucleotide, that is SEQ ID NO: 3.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a polynucleotide sequence having SEQ ID NO: 3. The subject matter which is claimed is described above. First, a determination of the level of predictability in the art must be made in that whether the level of skill in the art leads to a predictability of structure; and/or whether teachings in the application or prior art lead to a predictability of structure. The claims are directed methods which utilize polynucleotides to modulate the level of tocopherol in a plant. With regard to the elected invention, the specification provides only one proteins and a one cDNA encoding this protein within the scope of the instant claims, and does

not specifically teach or describe any other polynucleotides that are related to SEQ ID NO: 3 within the limitations of the rejected claims. The specification provides no guidance as to how or where the disclosed polynucleotide can be modified yet still maintain the functionality required for the instant methods. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. Therefore, there is a lack of guidance or teaching regarding structure and function because there is only a single example provided in the specification and because there is no guidance found in the instant specification.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

For the instantly rejected claims, only SEQ ID NO: 3 is described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate written description of polynucleotide which has nucleotides modified by addition, insertion, deletion, substitution or inversion with respect to SEQ ID NO: 3 but retaining correlative function in the claimed methods.

6. Claims 22-26 and 31-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (A) methods for increasing the level of polypeptides encoded by instant SEQ ID NO: 3 or instant SEQ ID NO: 9 in a plant, (B) methods for increasing the level of and tocopherols in a plant wherein either (A) or (B) include a step of transforming the plant with instant SEQ ID NO: 3 or SEQ ID NO: 9 in the sense orientation, does not reasonably provide enablement for methods which utilize other polynucleotides or methods which utilize SEQ ID NO: 3 or SEQ ID NO: 9 in the anti-sense orientation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is noted that with regard to specific sequences, a restriction requirement was set forth, and applicant elected methods which utilize SEQ ID NO: 3.

These claims are drawn to methods for modulating the level of tocopherol in a plant, comprising stably transforming a plant cell with a polynucleotide selected from the group consisting of (i) a polynucleotide comprising SEQ ID NO: 3, (ii) a polynucleotide that encodes SEQ ID NO: 4, from (iii) a polynucleotide having 70% sequence identity to SEQ ID NO: 3 or (iv) a polynucleotide which selectively hybridizes to SEQ ID NO: 3 under "stringent conditions" and a given wash condition, or the complement of any of these polynucleotides, said

polynucleotide operably linked to a promoter and growing the plant cell to regenerate a plant which has the appropriate component modified. All of the claims encompass methods wherein the transgene is introduced in either the sense or antisense orientation, with claim 25 specifically reciting that tocopherol is increased and claim 26 specifically reciting that tocopherol is decreased.

With regard to the instant claims, teaches soybean plants transformed with SEQ ID NO: 3 (i.e. the polynucleotide encoding SEQ ID NO: 4) in the positive (sense) orientation (see examples pages 55-71). Applicant provides the tocopherol/oil ration in somatic embryos produced from 33 different transformation events (pages 60-61). Applicant suggests that the normal range for such ratios would be from 2-5, and that the ratio would be higher than 5 if over-expression of the phytyl/prenyltransferase has increased the tocopherol production in the plants. Of the 33 ratios provided in Table 5, about a third of them were found to have tocopherol/oil ratios above the normal range. Applicant has thus demonstrated a method of increasing tocopherol levels in transgenic plants by transforming them with instant SEQ ID NO: 3, considering the ability of one to screen the transformed plant lines for the desired phenotype.

The specification has not provided any examples of methods for reducing the level of phytyl/prenyltransferase protein in a plant or methods for modulating the level of tocopherol in a plant that utilize transformation of plant cells with antisense constructs.

The state of the art for the isolation of cDNA or genomic clones with a defined functionality is highly unpredictable. With regard to SEQ ID NO: 3, applicant has isolated and characterized a single polynucleotides that is clearly involved in tocopherol synthesis, namely SEQ ID NO: 3, encoding SEQ ID NO: 4. Applicant has not demonstrated that any

polynucleotides that are modified with regard to SEQ ID NO: 3 (within the scope of the recited homology and hybridization language) retain the ability to increase tocophorol synthesis in plants. Thus, it is not clear that methods utilizing these genes would accomplish the goals set out in the preamble of these claims.

Moreover, it is noted that the instant claims encompass methods which utilize nucleic acids that are related to SEQ ID NO: 3 based on hybridization or homology. However, Applicant provides no guidance for the regions of the disclosed SEQ ID NO: 3 which are essential or sufficient to modify tocopherol production in transgenic plants. In the absence of such guidance, undue trial and error experimentation would be required to screen the vast number of different polynucleotides with 70% homology to or that would hybridize to SEQ ID NO: 3 to identify those which have the ability to modulate tocopherol in plants.

The state of the art for modification of gene expression or of phenotypic characteristics in plants by genetic transformation is highly unpredictable and hence significant guidance is required to practice the art without undue experimentation. It is clear from the specification that applicant is able to increase the level of instant SEQ ID NO: 3 or SEQ ID NO: 9 in transgenic plants, and that such an increase results in an increase in tocopherol production. However, the modulation of enzyme activity and achievement of a particular phenotype by antisense (also encompassed by the claimed methods) constructs is much less predictable. Indeed, the knowledge in the prior art would enable the skilled artisan to make transgenic plants with antisense constructs of SEQ ID NO: 3 or SEQ ID NO: 9, but it is highly unpredictable what effect these constructs would have on the transformed plant. The response of a transgenic plant to an antisense construct is dependent upon a number of factors, one is the sequence specific

hybridization of the antisense transcript to some expressed nucleic acid in the transformed plant. For example, Elomaa et al. (1996, enclosed herewith) teach that the degree of inhibition by an antisense transgene was dependent on homology between the antisense and the target genes. However, in the instant case, applicant has not provided any guidance as to what plants would contain sequences that are sufficiently homologous to instant SEQ ID NO: 3 or instant SEQ ID NO: 9 such that either of these would be successful at inhibiting the production of any target protein, let alone a target protein that would decrease the production of a phytyl/prenyltransferase protein or tocopherol. Furthermore, it is difficult to predict that an antisense construct will even decrease the production of any target of interest. For example, Colliver et al. teach an increase in transcripts following antisense transformation (1997, Plant Molecular Biology 35: 509-522, page 519, left column, second paragraph). Finally, even if inhibition of a transcript of interest was observed, it is highly unpredictable whether or not that inhibition will have the desired effect on the phenotype. For example, Majeau et al. teach that although antisense expression of a transgene resulted in 99% of carbonic anhydrase activity inhibition, this did not effect the CO2 assimilation, as would have been expected (Plant Molecular Biology, 1994, 25(3):377-85). In the instant case, applicant has even suggested that plants may contain more than one enzyme that has similar function to those encoded by instant SEQ ID NO: 3 or SEQ ID NO: 9. It is unpredictable whether these other enzymes may mask the effect of the antisense construct for example. In genetically modified plants, the introduced transgenes are sometimes not expressed, and they can also result in co-suppression effects. None of these effects are predictable, and the mechanisms of gene silencing are still not fully understood. Moreover, the phenotypic characteristics that will result from expression of a given

DNA construct cannot be reliably predicted. In fact, often the expected phenotypic result is not achieved. For example, the instant specification teaches that the blocking of the SLR1736 gene had no effect on plastoquinones when such effects would have been expected.

Given the unpredictability in the art of plant transformation to obtain a specified phenotype, the instant invention is not enabled given the lack of guidance in the specification with regard to what nucleic acids other than SEQ ID NO: 3 can be expected to result in a modulation of tocopherol levels in plants. In the absence of such guidance, undue trial and error experimentation would be required to screen through the myriad of different DNA constructs and the vast number of transgenic plants to determine how to carry out the methods of the claimed invention. When all of the above is weighed, it is concluded that undue experimentation would be required to practice the invention throughout the full scope of the claims.

Response to Remarks

The 112 2nd paragraph rejection is withdrawn in light of applicant's amendments to the claims.

Applicant points out that "the application discloses a structure via a DNA sequence (SEQ ID NO: 3) of an isolated polynucleotide whose overexpression increases the amount of tocopherol relative to oil in a plant tissue." This is not at issue, the examiner agrees that such a teaching has been provided, and states as much in the written description rejection. However, applicant does not disclose additional variants, homologues, and related sequences as encompassed for use within the instantly claimed methods.

Applicants argue that physical and chemical properties associated with the sequences utilized in the methods are defined by hybridization conditions to the disclosed sequence beginning on page 12, line 30 of the specification and structural variants are described in the specification at page 9, lines 7-21 such that the skilled artisan could readily visualize that the applicant was in possession of the invention claimed. The section of the specification cited at page 12 discussed typical hybridization conditions, and that at page 9 discusses very broadly discusses different types of variants that are possible. This is not a demonstration of possession of the invention, but instead a description of conditions for an assay and what may exist, as opposed to a demonstration of disclosure of what does exist. While the disclosure of nucleic acids used in the claimed method provides a description of a structure (i.e. having homology to instant SEQ ID NO: 3 or hybridizing to instant SEQ ID NO: 3), they do not provide a function that is correlative or predicted based on the modified structure from SEQ ID NO: 3.

The court has made it clear that with regard to chemical compounds, the standard for written description is possession, not enablement or intent to claim. "While we have no doubt a person so motivated would be enabled by the specification to make it, this is beside the point for the question is not whether he would be so enabled but whether the specification discloses the compound to him, specifically, as something appellants actually invented. We think it does not." In Re Ruschig, 379 F.2d 990, 995, 154 U.S.P.Q. 118, 123 (CCPA 1967). Furthermore, the court stated "Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." The Regents of the University of California v. Eli Lilly & Co., 43 U.S.P.Q.2d 1406 (Federal Circuit 1997). In the instant case, although applicant have provided a general descriptor of the polynucleotides to

be used in the instant invention and a beginning structure (i.e. a recited relationship to instant SEQ ID NO: 3) these even taken together are not sufficient to convey possession of the entire possible group of all of the nucleic acids that have 70% identity to or would hybridize to instant SEQ ID NO: 3 that are encompassed by the instant claims. The specification has not demonstrated a correlation between having homology to SEQ ID NO: 3 or hybridizing to SEQ ID NO: 3 and any particular activity. There is no such known correlation discussed in the specification nor disclosed that would lead the skilled artisan to be able to envision all of the members of the genus of nucleic acids that have 70% identity to or hybridize with instant SEQ ID NO: 3 and modulate the level of tocopherol in a plant.

Applicant argues that the examiner has misapplied Fiers v. Sugano in support of the rejection because the instant specification provides a complete DNA sequence and methods for isolating the sequence, citing the specification at page 42. The examiner agrees that the complete SEQ ID NO: 3 is described, but this is only a single representative of a broad genus as claimed for use in the instant methods. Applicant has not described the variants and homologues of SEQ ID NO: 3 that are claimed and are at issue. With regard to these sequences, the Fiers decision is certainly relevant because it addresses precisely the issue of claiming sequences that Applicant has not demonstrated that Applicant possesses.

Applicant suggests that the amendments to the claims have overcome the enablement rejection, but applicant does not provide any specific comments as to the factors of the enablement rejection that remain, even in light of the amended claims. For example, the claims

still encompass methods wherein the tocophorel levels in plants are decreases, said methods which are not supported by the specification (as discussed in the rejection) and the claimed method still encompass the use of a wide variety of nucleic acid sequences, also which are not enabled by the specification (as discussed in the rejection). Thus, the rejection is maintained as discussed herein.

Conclusion

7. No claims are allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Switzer whose telephone number is 703 306 5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on 703 308 1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703 305 3592 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 0196.

Juliet C. Switzer
Patent Examiner
Art Unit 1634

August 19, 2003

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